

# Patients' experiences of intervention trials on the treatment of myocardial infarction: is it time to adjust the informed consent procedure to the patient's capacity?

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## Abstract

**Objective**—To investigate how patients included in trials on treatment in the early phase of acute myocardial infarction experience the consent procedure.

**Design**—A combined qualitative and quantitative interview concerning the patients' knowledge of the trial, their feelings about being asked to participate, and their attitudes towards the consent procedure.

**Setting**—Tertiary referral centre.

**Patients**—31 patients who had given written informed consent for their participation in randomised intervention trials of acute myocardial infarction.

**Results**—The patients interviewed had only fragmentary knowledge about the trial they were involved in. Most considered that reading and signing a consent form was an unwanted or unnecessary procedure. Instead, they would have preferred to have been given concise verbal information about the study. Most were willing to allow a physician to decide for them in the event of their being too ill to be asked about their participation.

**Conclusions**—Patients who are asked to participate in intervention trials in the early phase of acute myocardial infarction often appear to lack sufficient knowledge to reach an autonomous choice. There were problems and disadvantages associated with the process of obtaining written informed consent in this particular situation, especially regarding the need for the patient to sign a consent form during the acute phase of the disease.

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Keywords: informed consent; clinical trial; acute myocardial infarction; patient attitudes

Dealing with the practical and ethical problems raised by enrolling patients in studies on acute myocardial infarction is part of the everyday clinical work in many cardiology departments. In order to recruit such patients to the earlier thrombolysis trials, only brief verbal information about the study was required.<sup>1-3</sup> However, following the adoption of the longer and more formal consent procedure employed in the USA, eligible patients in Sweden and most other European countries must now also receive comprehensive written information and sign a consent form before being included.<sup>4,5</sup> From our own experience, the standards necessary for inclusion are often criticised by the physicians involved. Comments like "It felt unethical to ask the patient to sign the paper when he was in such great pain" and "It is outrageous that we must do it this way" are not unusual. In other words, physicians are questioning whether patients who are under emotional and physical stress are capable of giving adequate informed consent for their participation in such studies, and the extent to which patients can be said to make a free choice when they are in a state of dependence on health care professionals.

These physicians' viewpoints or misgivings have, at least to a certain extent, turned out to be well founded. Previous studies on this topic have shown that many patients do not read the consent form before signing it and have little

recall of the consent process. Others do not even know that they are involved in a research project.<sup>6</sup> Some patients fear that refusal to give consent could affect their recovery.<sup>7</sup> However, most are willing to participate in clinical trials of treatment in myocardial infarction for the benefit of themselves and other patients.<sup>6,8</sup>

Consensus statements on how to proceed when conducting research in emergency situations deal primarily with patients from whom it is not possible to obtain informed consent in any form; they cannot thus be fully applicable to the circumstances of patients affected by acute myocardial infarction.<sup>9-11</sup> Such patients may have a wide range of symptoms, varying from severe pain and loss of consciousness to almost no symptoms at all.<sup>12,13</sup> This means that some of the patients lack competence and autonomous ability entirely, while others have a reasonable capacity to make an autonomous decision about their participation in a study. We feel that the concept of informed voluntary consent, seen from the perspective of patients with acute myocardial infarction, has not been fully elucidated and analysed.

Our aim in this mainly qualitative study was to investigate how patients included in trials of treatment in the very early phase of acute myocardial infarction experienced the consent procedure. On the basis of the interview results the following questions will be analysed and tentatively answered:

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- How should physicians proceed when they wish to include patients with acute myocardial infarction in intervention studies?
- Is research on this category of patients defensible even if informed consent cannot be obtained?

## Methods

### MATERIAL

Our aim was to obtain an informative and a varied sample (non-probabilistic sampling).<sup>14 15</sup> As a starting point, 30–50 interviewees were thought to be required for this mainly qualitative study in order to provide the answers we sought. When no further qualitative data could be obtained by increasing the number of interviews (theoretical saturation), no more interviews would be conducted.<sup>16</sup> This determined the final size of the study group ( $n = 31$ ).

Patients who had given their written, informed consent for participation in ongoing randomised intervention trials of acute myocardial infarction at the department of cardiology, Sahlgrenska University Hospital, between March 1998 and May 1999 were selected for the study. After being given verbal and written information about the purpose of the research interviews, none of the patients approached declined to participate. However, three eligible candidates were excluded owing to their poor or unstable condition following the acute phase of their infarction. The study group consisted of 31 patients, 22 men and nine women, recruited from ASSENT II (assessment of the safety and efficacy of a new thrombolytic agent), CADILLAC (controlled abciximab and device investigation to lower late angioplasty complications), and ASSENT PLUS. The median age was 69 years (range 46–85 years). Seven patients had an educational level higher than compulsory schooling. None had previously participated in research on acute care.

The median score given by the patients to estimate their pain on arrival at hospital (on the 10 point visual-analogue scale (VAS)) was 5, with a range from 1–10. In ASSENT II, conventional treatment with the 90 minute infusions of the thrombolytic substance tPA (alteplase) was compared with the more developed TNK-tPA (tenecteplase) product, given as a single injection. In CADILLAC, which had factorial design, percutaneous transluminal coronary angioplasty (PTCA) with or without stent implantation and with or without abciximab were compared. The follow up period lasted for 12 months and included a second coronary arteriogram after seven months. In ASSENT PLUS, the thrombolytic treatment with tPA was given together with heparin infusions for 48 hours, or low molecular weight heparin-dalteparin were given subcutaneously for 4–7 days. Coronary arteriography was performed at some point between day 5 and day 7.

### INTERVIEWS

Semistructured qualitative interviews with open ended questions were preceded by pilot interviews.<sup>17</sup> The patients were asked about

Table 1 Distribution of the answers to the two structured questions

What type of information do you feel it is necessary to provide when enrolling patients with heart attacks in this kind of treatment study?	
Verbal	26
Verbal and written	2
Uncertain	3
How do you feel one should proceed if you were too ill to be asked to participate in a study of this kind?	
Let the physician decide	26
Refrain from research	1
Uncertain	4

their knowledge of the trial in which they had participated, about their experiences and feelings over being included, and their attitudes towards the consent procedure. These predetermined themes were judged to measure relevant aspects of the concept of informed consent in the context of acute myocardial infarction. The qualitative raw data, which consisted of notes made during the interviews, were subjected to content analysis and organised into conceptual categories by AA and GH.<sup>18</sup> These categories are presented below as headings, each being explained and illustrated by examples of quotes from the patients' responses. To clarify the patients' views further, two structured questions with fixed alternative answers were incorporated into the interview:

- (1) "What type of information do you feel it is necessary to provide when enrolling patients with heart attacks in this kind of treatment study?" (verbal/verbal and written/uncertain).
- (2) "How do you feel one should proceed if you were too ill to be asked to participate in a study of this kind?" (refrain from research/let the physician decide under the condition that the research has been approved by a research ethics committee/uncertain).

The distribution of the answers to the two structured questions is shown in table 1. The interviews, which varied in length from 15–40 minutes (median 20 minutes), were all performed by the same person (AA) while the patients were still on the ward, 2–5 days after their admission to hospital.

The study was approved by the local research ethics committee.

## Results

### PATIENTS' ESTIMATE OF THEIR ABILITY TO UNDERSTAND THE INFORMATION INCLUDED IN THE CONSENT PROCEDURE

#### *In a state of mind in which the capacity to understand was severely diminished*

If the definition of a competent person is one who is able to understand the research procedure, to deliberate about the major risks and benefits, and to make a decision in the light of this deliberation,<sup>19</sup> hardly any of the respondents were judged competent. Most interviewees felt that they either had too low a level of consciousness to understand the information given, or were in too much pain to bother, as illustrated by statements like:

"I did not catch what he said. I signed without understanding anything."

"They asked me if I wanted to take part and I wrote down my name. I did not read what I signed. I didn't care because of my pain."  
 "I tried to read the information but I didn't get it."

#### *Too little time to deliberate the decision*

The quotations below suggest that the patients' felt they had too little time. In the discussion we shall return to the conclusions that can be drawn from such statements.

"I was under stress. They had to do it within a certain time frame, otherwise my opportunity to participate was gone."

"There was not enough time for me to receive enough information. The only thing left to do was to join in."

#### *Having the competence to understand*

All the interviewees had been informed (most probably to a varying degree and in various ways) and had given consent for their participation in one of the trials. However, very few patients indicated by their stories that they considered themselves competent to understand the information or to be able to make an autonomous decision in the particular situation; for example: "I'm satisfied with the information I got. It was not a difficult decision for me to make after that." We did not evaluate further whether patients' feelings of incompetence also meant that they lacked the ability to make a "valid decision" in this respect.

#### PATIENTS' COMPREHENSIONS ABOUT THE PURPOSE OF THE STUDY

##### *Comparisons between treatments/methods*

The most common descriptions of the purpose of the study given by the interviewees dealt with the comparative aspect:

"All I remember was that there were two equally good clot dissolving preparations A and B. That (information) was sufficient for me to say 'I'm in'."

"It was about following up two different methods. The lottery would decide if I would get a net or not. Did I get a net?"

##### *Improvement of the treatment of myocardial infarction*

This impression was expressed in general terms such as:

"I understood that the aim of the study was to find out something which could be of value for the treatment of heart attacks."

"They wanted to know what would be the best for the future. For me the details are unimportant."

Other patients, however, were more specific in their comments concerning the purpose of the study and focused on the development of medical devices:

"I got the impression that I would be testing a net."

"It had to do with the development and improvement of the net. They should last longer and be safer, something like that."

#### *Hardly any knowledge or no knowledge at all*

According to some of the patients their knowledge about the study was almost non-existent:

"The only thing I remember was that they asked me about a study, which dealt with dissolving blood clots faster."

"I only remember that I felt so bad that I thought I was dying."

Moreover, two patients did not know that they had been included in a study at all, as illustrated by the quote:

"I was not aware of the fact that it (the information) was about a study."

#### FEELINGS ABOUT BEING ASKED TO GIVE WRITTEN INFORMED CONSENT TO PARTICIPATE IN THE STUDY

##### *Being subjected to an unwanted procedure*

"I consider it unnecessarily brutal to put a paper under your nose when you don't even know where you are. You can't really make any decisions. That detail (the signing) is unnecessary, ethically incorrect."

##### *Being the subject of an experiment and/or being in a situation where you have no real choices*

"I felt like a guinea pig and I signed the paper with some hesitation. It was unpleasant to be seen as the subject of an experiment. I was only interested in helping myself."

"What alternative did I have? Who could say no? I thought, here I am in a condition like this and being used as a guinea pig."

"Even though I did not perceive it (the study) as something threatening, I did not really have a choice. I was also against being subjected to lottery."

##### *Becoming involuntarily responsible for the choice of treatment*

"I got the idea that they handed over the decision of which treatment to choose to me."

"The doctor asked me to decide what he should do. Afterwards he said to me that I had made the right decision."

These misconceptions are obvious evidence of how little of the information the patients understood.

##### *Taken by surprise*

"It felt strange to sign when I didn't know what I was signing, I had received so much morphine that I did not know what I signed. I find it strange that they asked me when I was in such bad condition."

"I was a bit taken by surprise and felt a bit belittled by their request but I do not want to criticise."

##### *Neutral reactions and indifference*

"They wanted a signature and they got one. It doesn't matter to me."

"Actually, to me it doesn't matter. Of course you can inform me if it's necessary."

*Acceptance considering the legal aspects*

Some of the interviewees looked at the procedure from the perspective of the doctor. They accepted the proceeding as a mandatory step in order to avoid legal conflicts.

"I guess it is necessary to follow the rules in order to avoid a civil case."

"Wouldn't a witness have been equally good, seen from a legal point of view?"

"I guess it is for your own good, just to assure that you don't get into trouble."

*Positive reactions*

Certain positive reactions arose along with the patients' reasons for consenting. The two main reasons given for participating in research were hopes of obtaining better treatment and an altruistic willingness to help others:

"I considered it an advantage (to take part in the study). I knew it was for my own good and for future patients. I have a daughter who is doing research. I know how important it is."

"I am always positive towards that kind of thing. I want to contribute to research. When somebody asks me, I will always do what I can."

"I thought it sounded positive because you were offered a better follow up programme. You will also be of help to others."

#### ATTITUDES TOWARDS PARTICIPATION IN RESEARCH WHEN THERE ARE DIFFICULTIES IN OBTAINING INFORMED CONSENT

*A general acceptance of participation in research based on the trust of physicians*

"I take it for granted that the specialists do what they feel is best for me. I rely on the Swedish health care system."

"You could have done what you thought was the best thing to do. It is alright if you inform me afterwards."

"The doctors wouldn't do anything that makes matters worse."

*Acceptance of allowing physicians to decide without having to ask the patient, because of the patient's lack of knowledge*

"I would not mind if you did tests without asking me. The patient doesn't understand."

"The patient can't decide and he or she doesn't have enough knowledge. All research is good. One should entrust these matters to the experts."

*Acceptance of handing the decision over to physicians after they have done what they can to respect the autonomy of the patient*

"If you are clear in your mind you should be asked. One should not hand over the responsibility to relatives. If you can't ask, the physicians should be allowed to decide and they have to take the consequences."

"Where the patient is unable to say yes or no and there are no relatives present, the doctors should be allowed to step in and make the decision. Otherwise it should be considered a form of self defence to have the opportunity to say no."

*Indifference*

"If you can ask, that's good. If not, you can decide by yourself."

"It really doesn't matter if I know about it (being included) for my own sake."

"I thought it seemed reasonable to sign the paper."

*Negative attitudes*

Only one of the interviewees was against research if consent could not be obtained. He argued that "it is unethical not to let the patient decide."

## QUANTITATIVE RESULTS

Twenty six of the interviewees (84%) would prefer only verbal information and consultation when deciding whether or not to participate in a study (table 1). Among the remainder, two also wanted written information to be included in the consent procedure, while three were not sure of their opinion. The majority ( $n = 26$ ) of the interviewees felt that the physician alone should be able to decide to include a patient with acute myocardial infarction in a trial when the patient was too ill to be asked for consent to participate in the study. Only one of the patients interviewed was against research being performed under conditions where the patient lacks the capacity to give informed consent.

**Discussion**

Our main purpose in this study was to describe experiences, feelings, and attitudes among patients included in intervention studies of treatment for myocardial infarction. This qualitative approach involving a small number of patients selected from one university hospital does not allow us to make generalisations about all patients in this situation. One major reservation that has to be made—though we find it improbable—is that the consent procedure could have been dealt with less well in this particular department of cardiology than in others. It could thus be argued that patients in other hospitals might have been better placed to understand the issues involved, in which case we would need to improve our ability in that respect rather than questioning the approach involved in obtaining consent. Nevertheless, we consider our data to be relevant to the issue and sufficient to allow analysis of the concept of informed consent in the context of acute myocardial infarction—including the possible problems and disadvantages associated with the consent procedure which in our view need to be debated.

#### HOW SHOULD PHYSICIANS PROCEED IN SUCH INTERVENTION STUDIES?

All possible measures to increase the autonomy of the patient under the prevailing circumstances should be taken and tried. This includes optimising medical treatment aimed at relieving pain and other distressing symptoms. Provided that health care staff act in a professional and respectful way, patients are likely to place their trust in them. This trust is a fundamental or necessary condition for the creation of an "autonomous atmosphere," in



which the patient feels free and safe to make decisions or leave them to others. The majority of the patients interviewed preferred summary verbal information and wanted to be spared the signing of a paper which they had not read and the content of which was unfamiliar to them. Some were astonished at or even indignant about such a procedure, which they considered unnecessary, strange, or even unethical. Several of the interviewees also said spontaneously that they regarded signing the consent form as something they did for the sake of the physician. Thus, instead of requiring patients to read consent forms and asking for signatures, physicians should perhaps devote more time to providing patients and relatives with clear and concise information, focusing on a few essential aspects of the study. This information could be supported by simple but descriptive illustrations.

On the basis that the patients interviewed here understood only basic information at most, we think it would be appropriate and generally sufficient to ask something along the following lines: "Are you willing to take part in a study where we are comparing two drugs which are used for the treatment of heart attacks, so that we can find out which one is best? You are free to say no. In that case you will receive standard care. If you want, we can provide you with more information now. Otherwise, we will give you more information about the study later when you feel better."

To summarise, in the early phase of acute myocardial infarction, it could be defensible to inform the patients very briefly about the ongoing research. However, as soon as possible the patients should be fully informed about the complete research protocol and their right to either consent to or decline further participation. We feel that the requirement to obtain the patient's signature on the consent form is debatable for ethical reasons. Is this an unwarranted procedure which only places an additional burden on the patients and physicians concerned? Moreover, it seems a reasonable claim that the primary aim of this procedure is to make sure that those responsible for the study avoid any legal inconvenience.

If it becomes clear that a patient lacks competence to make a morally acceptable autonomous decision, one should consider the alternatives. If family members are present in the acute situation, they should be asked if they think the patient would agree to participate. When they have been adequately informed about the study they should themselves be asked how they view the request to involve the patient. This does not mean that they should be forced to make the final decision. If family members remain hesitant or do not want the patient to participate, the patient should not be included, but should be given the best treatment available outside the scope of the study.

IS RESEARCH ON THIS CATEGORY OF PATIENTS  
DEFENSIBLE EVEN IF INFORMED CONSENT  
CANNOT BE OBTAINED?

Ethical codes and declarations of ethics have been developed for research on human

subjects.<sup>20-22</sup> This has been done in order to protect the basic human rights of patients and to maintain the credibility of investigators and society as a whole. The main aim is to ensure that patients obtain adequate information before making an informed decision, and that they are free from coercive influences when deciding whether to participate in research or not.

As we have shown, patients suffering from acute myocardial infarction are often unable to make autonomous choices. The majority of the interviewees said that they either had too low a level of consciousness to understand the information given about the study, or were in too much pain to bother. Some felt they were in a situation where they had no real choice, others that they should have had more time to consider their participation. The patients interviewed had a very limited and fragmentary knowledge of the purpose of the trial in which they were participating, and to which they had given their consent. Many of them had an incorrect perception of the aims of the trial, despite the fact that they had been given the opportunity to read the accompanying written information over several days. Thus the results of our study suggest that many patients were included on doubtful grounds, at least if it is claimed that a certain amount of competence and understanding is necessary for free and informed consent to be obtained. The fact that many patients who have participated in clinical trials on acute myocardial infarction fail to understand the research protocols fully has been shown in other studies as well.<sup>23-24</sup> We should be asking whether patients with acute myocardial infarction are competent to make valid decisions about study participation before considering their enrolment in therapeutic research. However, it is a delicate matter to decide whether the patient lies above the lowest acceptable level in that respect. Confidence in Swedish physicians seems high, which probably contributes to the fact that most of the patients were willing to allow, or even wanted, their physicians to decide for them—at least if they were to be too ill to be asked about participation in research.

We do not mean to imply that one should abandon the consent requirements for patients with acute myocardial infarction generally, but we feel it is time to debate the procedure in the light of the responses reported in this study. Perhaps we have to face the following choices. Either one does not conduct research at all on patients with acute myocardial infarction suffering from the more severe symptoms, or one is willing to accept that only a low level of competence is necessary for making an autonomous decision over participation, or one must consider doing research even without the subjects' consent. The early phase of acute myocardial infarction may be compared with other conditions in emergency medicine and critical care, where research can be conducted without obtaining consent if certain conditions prevail.<sup>9-25-27</sup> The importance of discussing this ethical research question thoroughly is emphasised by the fact that we are in a pre-hospital

treatment era for acute myocardial infarction. The saying "time is muscle" is familiar to all cardiologists, and this medical aspect should be considered when formulating rules for obtaining patients' permission in randomised trials of treatment. Even though one study has indicated that while the time to treatment of myocardial infarction in an emergency department was not delayed by a thrombolysis research trial, there is undoubtedly a risk that formal consent procedures could prolong door to treatment time.<sup>28</sup>

#### CONCLUSIONS

The results of this study raise questions about whether patients in the early phase of acute myocardial infarction have the capacity to make morally autonomous choices about their participation in intervention trials. The interviewees had only fragmentary knowledge about the trial to which they had given their consent. Most preferred summary verbal information and wanted to be spared the need to sign a consent form which they had not read and struggled to understand. We feel that it is time to adjust the informed consent procedure to the patients' capacity in this particular situation. If patients have confidence in their physicians and positive attitudes towards participation in research, then perhaps what really matters is not the information itself but that their right to say yes or no is respected. In addition, there should be debate over whether there are ethically justified alternatives when suitable patients are not capable of giving truly informed consent to their participation in a research project. Surveys that address attitudes to these questions among the general public, patients, ethics committees, and the scientific community should be undertaken.

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